Attorney's Docket No.: 03678.0022.CNUS02

In the Claims

1. (Previously Presented) A compound of Formula IIIA:

Formula IIIA

wherein:

X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m = 0, 1, 2, 3, or 4;

B is a purine or a pyrimidine residue linked through the 9- or 1-position, respectively;

 $Z = OH \text{ or } N_3;$

 $Z' = OH \text{ or } N_3;$

Y = H or OH;

Y' = H or OH;

provided that when Z is N₃, Y is H or when Z' is N₃, Y' is H;

 R_4 is hydroxy, amino, cyano, aralkoxy, C_{1-6} alkoxy, C_{1-6} alkylamino, or dialkylamino; R_5 is hydrogen, acyl, C_{1-6} alkyl, phenyloxy, C_{1-5} alkanoyl or absent;

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 R_6 is oxo, hydroxy, mercapto, C_{1-4} alkoxy, C_{7-12} arylalkoxy, C_{1-6} alkylthio, amino, C_{1-5} disubstituted amino, triazolyl, C_{1-6} alkylamino or di- C_{1-4} alkylamino, where the alkyl groups is optionally linked to form a heterocycle or link to N^3 to form a substituted ring; or

R₅ and R₆ taken together form a 5-membered fused imidazole ring between positions 3 and 4 of the pyrimidine ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C₁₋₄alkyl, phenyl, or phenyloxy, which themselves are optionally substituted;

 R_7 is hydrogen, hydroxy, cyano, nitro, substituted and unsubstituted C_{2-8} alkenyl, phenyl, substituted and unsubstituted C_{2-8} alkynyl, halogen, CF_3 , substituted and unsubstituted C_{1-6} alkyl, allylamino, bromovinyl, ethyl propenoate, propenoic acid; or

R₆ and R₇ taken together form a 5 or 6-membered saturated or unsaturated ring bonded through N or O at R₆, such ring optionally contain substituents that themselves contain functionalities;

 R_8 is hydrogen, amino or di- C_{1-4} alkylamino, C_{1-4} alkoxy, C_{7-12} arylalkoxy, C_{1-4} alkylthio, C_{7-12} arylalkylthio, carboxamidomethyl, carboxymethyl, methoxy, methylthio, phenoxy or phenylthio; provided that when R_8 is amino or substituted amino, R_7 is hydrogen;

provided that when B = adenine, adenine 1-oxide, or $1,N^6$ -ethenoadenine, then:

- (a) $R_6 \neq \text{oxo when } R_4 = \text{oxo}, Y = Z = OH \text{ and } R_5 = R_7 = R_8 = H$;
- (b) $R_7 \neq Br$ when $R_4 = R_6 = oxo$, Y = Z = OH, and $R_5 = R_8 = H$;

provided that when B = adenine, then:

- (a) $R_6 \neq$ amino when $R_4 = \infty$, Y = Z = OH, R_5 is absent, $R_7 = R_8 = H$, and n + m = 0, 1, or 2;
- (b) $R_7 \neq CH_3$ when $R_4 = R_6 = oxo$, Y = H, Z = OH, and $R_5 = R_8 = H$;
- (c) $R_7 \neq F$ when $R_4 = R_6 = 0$ xo, Y = H, Z = OH, $R_5 = R_8 = H$ and n + m = 2;

provided that when B = thymine, Y'= H and Z' = N_3 ; then $R_7 \neq F$, when $R_4 = R_6 = \infty$ 0, Y = OH, Z = OH, $R_5 = R_8 = H$, and n + m = 0; provided that when B = thymine, Y' = H and Z' = N_3 ; then $R_7 \neq CH_3$ when $R_4 = R_6 = 0$

oxo, Y = H, $Z = N_3$, $R_5 = R_8 = H$, and n + m = 0;

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provided that when B = guanine, then:

(a) $R_6 \neq \text{oxo when } R_4 = \text{oxo}, Y = Z = OH, R_5 = R_7 = R_8 = H \text{ and } n + m = 1 \text{ or } 2;$

(b) $R_6 \neq$ amino when $R_4 = 0x0$, Y = Z = 0H, R_5 is absent, $R_7 = R_8 = H$, n+m=1 or 2;

provided that when B is uridine, or 5-Br-uridine, then

(a) $R_6 \neq \text{oxo when } R_4 = \text{oxo}, Y = Z = OH \text{ and } R_6 = R_7 = R_8 = H$;

(b) $R_7 \neq Br$ when $R_4 = R_6 = oxo$, Y = Z = OH, and $R_5 = R_8 = H$;

provided that when B is 5-FU, then $R_7 \neq F$, when $R_4 = R_6 = 0x0$, Y = H, Z = OH, $R_5 = R_8 = H$, and n + m = 0;

provided that when B is cytosine, then $R_6 \neq$ amino, when $R_4 = \infty$, Y = Z = OH, R_5 is absent, $R_7 = R_8 = H$, and n + m = 1, or 2; and

provided that when B is cytosine, then $R_6 \neq \infty$, when $R_4 = \infty$, Y = Z = OH and $R_6 = R_7 = R_8 = H$, and n + m = 2.

2. (Original) A compound according to Formula IIA:

FORMULA IIA

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wherein:

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X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m= 0, 1, 2, 3, or 4;

B is a purine residue linked through the 9- position;

Z = OH or N<sub>3</sub>;

Z' = OH or N<sub>3</sub>;

Y = H or OH;

Y' = H or OH;

provided that when Z is N<sub>3</sub>, Y is H or when Z'is N<sub>3</sub>, Y' is H;
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 R_1 is H, C_{1-8} alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{6-10} aryl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C_{1-4} alkyl and when doubly substituted, the alkyl groups are optionally linked to form a heterocycle; or $A(C_{1-6}$ alkyl)CONH(C_{1-6} alkyl)B wherein A and B are amino, mercapto, hydroxy or carboxyl;

R₂ is O or is absent; or

 R_1 and R_2 taken together forms a 5-membered fused imidazole ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C_{1-4} alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{6-10} aryl, arylalkyl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C_{1-4} alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; and

 R_3 is H, C_{1-8} alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{6-10} aryl, carboxy, cyano, nitro, sulfonamido, sulfonate,

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phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C_{1-4} alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; C_{7-12} arylalkyl; C_{1-4} alkylamino, phenylamino,

 C_{7-12} arylalkylamino, C_{1-4} alkoxy, or C_{7-12} arylalkyloxy; C_{1-4} alkylthio, phenylthio,

 C_{7-12} arylalkylthio, or -A(C_{1-6} alkyl)CONH(C_{1-6} alkyl)B- wherein A and B are independently amino, mercapto, hydroxy or carboxyl;

provided that $R_1 \neq H$, when X is oxygen, methylene, or difluoromethylene, Y is OH, B is adenine, R_2 is absent, and R_3 is hydrogen;

provided that $R_1 \neq H$, when n + m = 2, X is oxygen, Y is OH, B is adenine, R_2 is absent, and R_3 is bromo, or 6-aminohexyl;

provided that $R_1 \neq H$, when n + m = 2, X is oxygen, Y is H, B is adenine, R_2 is absent, and R_3 is H;

provided that $R_2 \neq 0$, when n + m = 2, X is oxygen, Y is OH, $R_1 = R_3 = H$, and B is adenine, adenine 1-oxide, or $1,N^6$ -ethenoadenine;

provided that R_1 and R_2 do not form a 5-membered fused imidazole ring, when n + m = 2, X is oxygen, Y is OH, R_3 is H, and B is adenine, adenine 1-oxide, or ethenoadenine.

- 3. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the D- configuration.
- 4. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the L- configuration.
- 5. (Previously Presented) A pharmaceutical composition comprising a compound of Formula IIIA or IIA as described in Claim 1 or 2, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier therefor.

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6. (Previously Presented) A method of treating chronic obstructive pulmonary diseases in a mammal by administering an effective chronic obstructive pulmonary disease treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

- 7. (Previously Presented) A method of treating sinusitis, otitis media or nasolacrimal duct obstruction in a mammal by administering an effective mucus secretion clearing amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.
- 8. (Previously Presented) A method of treating dry eye in a mammal by administering an effective dry eye treatment amount of a compound of Formula III A or IIA as described in Claim 1 or 2.
- 9. (Previously Presented) A method of treating retinal detachment in a mammal by administering an effective retinal detachment treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.
- 10. (Currently Amended) A method of facilitating sputum induction in a mammal by administering an <u>effective</u> amount of a compound of Formula <u>IA or IB IIIA or IIA</u> as described in Claim 1 or 2, effective to facilitate sputum induction.
- 11. (Currently Amended) A method of facilitating expectoration in a mammal by administering an <u>effective</u> amount of a compound of Formula <u>IA or IB IIIA or IIA</u> as described in Claim 1 or 2, effective to facilitating expectoration.
- 12. (New) A method of treating cystic fibrosis in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to treat cystic fibrosis.

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(New) The method according to Claim 12, wherein said compound is P^1 -(2'-13. deoxycytidine 5'-)-P⁴-(uridine 5'-)tetraphosphate.